3-22-2017

Outcomes in Necrotizing Enterocolitis (NEC) Treated with Granulocyte Colony Stimulating Factor (GCSF) and Intravenous Immunoglobulin (IVIG) vs Standard of Care Alone: RCT Interim Safety Analysis

Sanjeet Panda
New York Medical College

Courtney Briggs-Steinberg
New York Medical College

Brian DeBenedictis
New York Medical College

Sri Narayana
New York Medical College

Edmund F. La Gamma
New York Medical College

Outcomes in Necrotizing Enterocolitis (NEC) Treated with Granulocyte Colony Stimulating Factor (GCSF) and Intravenous Immunoglobulin (IVIG) vs Standard of Care Alone: RCT Interim Safety Analysis

Sanjeet Panda MBBS, Courtney Briggs-Steinberg DO, Brian DeBenedictis MD, Sri KP Narayana MD, Edmund LaGamma MD
Division of Newborn Medicine, Maria Fareri Children's Hospital - NYMC, Valhalla, NY, United States

Background

- The incidence of necrotizing enterocolitis (NEC) is < 15% in ELBW neonates & is associated with > 25% mortality; medical management has not changed for the past 40 yrs.
- GCSF increases the absolute neutrophil count, improves neutrophil function (↑ Fc & C' receptor density) and lowers TNFα.
- IVIG improves phagocytosis, oxidative burst and opsonization activity.
- GCSF induced phagocytosis improves further in vitro when opsonized with IgG, we hypothesized that combining the interventions will improve neonatal outcomes with Bell stage II NEC.

Objectives

We seek to determine whether GCSF+IVIG augmented standard of care improves survival & expedites recovery vs standard of care therapy (SRx) alone in preterm neonates (<37 wks) with pneumatosis (Bell Stage II).

Methods

- IRB approved, parent consented, single center prospective, RCT of any preterm neonate who developed NEC at our NICU since Oct 2011.
- Neonates are randomly assigned to either SRx or treated with GCSF (10 mcg/kg/d) and IVIG (500 mg/kg/d) IV x 3d along with SRx.
- The primary outcome is survival to one month or the ability to attain full enteral feeds within 3 weeks of antibiotics.
- Serial blood counts are monitored on days 0, 1, 2, 3 & 7-10d.
- RCT interim safety analysis was done by paired t-test and chi-square.

Demographics

	Standard n=12	Treated n=17
Gestational Age (wks) Mean ± SEM (median, Min-Max)	27 ± 0.5 (27, 25-30)	28 ± 0.7 (28, 24-34)
Birth weight (g)	1017 ± 68 (1005, 600-1510)	1007 ± 95 (1030, 430-2120)
SGA %(n)	0 (0)	24 (4)
Antenatal Steroids %(n)	83 (10)	82 (14)
Male %(n)	75 (9)	24 (4)*

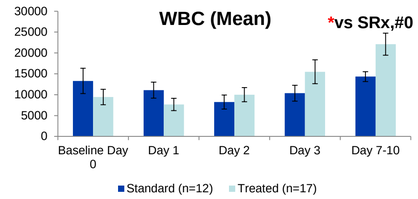
Clinical Characteristics at Onset

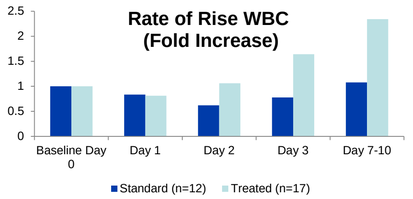
	Standard n=12	Treated n=17
DOL @ NEC (d) Mean ± SEM (Median, min-max)	20 ± 3.7 (17, 6-36)	23 ± 4.9 (21, 9-64)
PCA @ NEC (d)	30 ± 0.8 (30, 27-34)	31 ± 0.8 (31, 28-37)
Weight @ NEC (g)	1287 ± 140 (1260, 770-1910)	1272 ± 129 (1270, 680-2240)
Positive blood culture %(n)	8 (1)	12 (2)
HCT 48hrs prior to NEC	32 ± 1.3 (32, 27-41)	35 ± 2.7 (33, 24-57)
Presence of PDA %(n)	50 (6)	47 (8)
Treatment with Indomethacin %(n)	42 (5)	24 (4)
Full Oral Feeds %(n)	50 (6)	76 (13)
Feeding with Formula %(n)	50 (6)	53 (9)
Ventilator Dependent %(n)	25 (3)	23 (4)

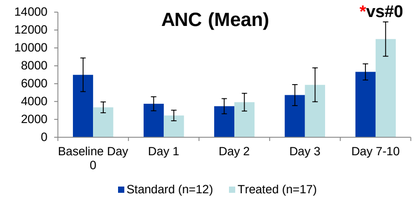
Clinical Outcomes at Discharge

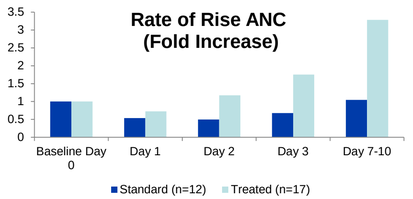
	Standard n=12	Treated n=17
Surgery %(n)	50 (6)	35 (6)
Death at 1 week %(n)	8 (1)	12 (2)
Death at 1wk- 1 month	0	0
Days to full feeds after NEC mean ± sd (median)	16 ± 7 (13)	21 ± 17 (14.5)
Full feeds within 3 wks of antibiotics %(n)	83 (10)	71 (12)
Primary outcome (Survival or attain full feeds within 3weeks) %(n)	92 (11)	88 (15)
Time discharge (days) mean ± sd (median)	91 ± 37 (83)	102 ± 42 (108)

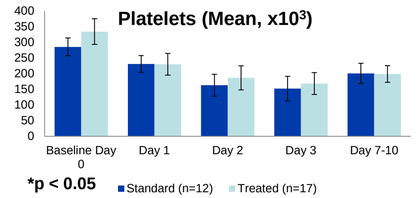
Hematologic Results

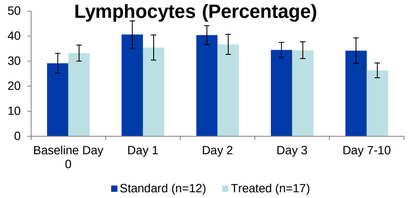












Conclusions

- There was no increase in complications (ROP,IVH,PVL and death) indicating the trial can continue. We plan to sustain enrollment to reach the desired goal of 25 subjects in each group.
- In the interim analysis we have not found statistically significant differences in our primary outcome.
- GCSF+IVIG increased WBC and ANC significantly even in critically ill neonates, rate of rise more then standard treatment.
- No effect on platelet and lymphocyte counts in either group.

References

1. Kocherlakota P and LaGamma E, Pediatrics1997:100e6
2. La Gamma & Decastro . Acta Pediatric sup 2002:10-116
3. Song, Subbrao and Maheswari. J Matern Fetal Neonatal Med. 2012
5. Kocherlakota, Narayana, Blau & Edmund F. La Gamma. White Blood Cell Changes Following Treatment with a Combination of Recombinant Human Granulocyte Colony Stimulating Factor (rhG-CSF) and Intravenous Immunoglobulin (IVIG) in Necrotizing Enterocolitis (NEC): In press: Pediatrics Infectious Disease Journal.